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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,969	08/21/2003	Roderic M.K. Dale	09388.0003-03	7575

21971 7590 06/22/2007

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EXAMINER	
CHEN, SHIN LIN	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
06/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,969	DALE ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 21 August 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 8-21-03 & 3-16-05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' preliminary amendment filed 8-21-03 has been entered. Claims 2-31 have been canceled. Claim 1 is pending and under consideration.

Specification

The disclosure is objected to because of the following informalities: The term, "CLAIMS" on page 37 is improper. Changing the term "CLAIMS" to "We claim:" or "What is claimed is:" would be remedial.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of bacterial growth of *Streptococcus aureus* and *Pseudomonas aeruginosa* by using a modified protonated oligonucleotide of SEQ ID No. 1 (9mer) consisting of 2'-O-methyl substituted ribonucleotides phosphodiester and with both 3' and 5' butanol end-blocking under a pH of 1-4.5 *in vitro*, the treatment of *Strep. pyogenes* skin infection on a dog by using a modified protonated SEQ ID No. 2 (12mer) under pH 1.5, and treatment of *Pseudomonas* burn wound on a BALB/c mouse by using disclosed protonated monomer or oligomer to reduce *P. aeruginosa* infection *in vivo*, does not reasonably provide enablement for a wound dressing

comprising any protonated nucleic acid, including polymer, oligomer and monomer, under any pH value. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claim is directed to a wound dressing comprising a solid substrate and a formulation of protonated/acidified nucleic acid.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). See also In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification of the present application discloses the inhibition of bacterial growth of *Streptococcus aureus* and *Pseudomonas aeruginosa* by using a modified protonated oligonucleotide of SEQ ID No. 1 (9mer) under a pH of 1-4.5 *in vitro*, the treatment of *Strep. pyogenes* skin infection on a dog by using a modified protonated SEQ ID No. 2 (12mer) under pH 1.5, and treatment of *Pseudomonas* burn wound on a BALB/c mouse by using disclosed

protonated monomer or oligomer (pH 1.5) to reduce *P. aeruginosa* infection *in vivo* (Examples 2-4). The claims encompass a wound comprising any protonated/acidified nucleic acid, including polymer, oligomer and monomer, either modified or not modified under any pH value.

The specification states "[t]he present invention provides devices and compositions for the management of infection of topical wounds and lesions wherein the device and compositions are given broad spectrum antibacterial properties by means of protonated/acidified nucleic acids" (page 3, lines 11-13). The wound dressing must have a use, which is wound healing via antibacterial activity by means of protonated/acidified nucleic acids. The claims read on a wound dressing comprising any protonated/acidified nucleic acid either modified or unmodified, under any pH value and said protonated/acidified nucleic acid on the wound dressing exhibits wound healing activity and reduce or prevent bacterial infection in light of the specification of the present application. It was unpredictable at the time of the invention whether any protonated/acidified nucleic acid having various sizes and under different pH value would have antibacterial activity such that the claimed would dressing would have wound healing function. The specification of the present application discloses the inhibition of bacterial growth using modified nucleic acids under a pH of 1.5-4.5 *in vitro* or *in vivo*. The specification fails to provide adequate guidance for using a protonated nucleic acid under a pH greater than 4.5 to inhibit bacterial growth *in vitro* or *in vivo,* such that the wound dressing provides their function in wound healing. As per the specification of the parent application 09/222,009, the pH value of the modified nucleic acid plays an important role in the inhibition of bacterial growth *in vitro*. The specification of the present application also points out that "nucleic acid preparation near pH 2 to 1 demonstrate better antibacterial activity than nucleic acids at or near pH 4.5"

(specification, p. 14, lines 2-3). The specification fails to provide adequate guidance and evidence for whether the protonated/acidified nucleic acids with a pH larger than 4.5 could still have the biological activity to inhibit bacterial growth either *in vitro* or *in vivo* such that the wound dressing would provide their function in wound healing. There is no evidence of record that a wound dressing comprising a solid substrate and any protonated/acidified nucleic acid, such as a polymer, an oligomer or a monomer, having a pH value higher than 4.5 would have a use, such as biological activity to inhibit bacterial growth either *in vitro* or *in vivo* such that the wound dressing would provide their function in wound healing.

The claim encompasses modified and unmodified protonated/acidified nucleic acid of various sizes. The specification also fails to provide adequate guidance for whether any unmodified protonated/acidified nucleic acid would exhibit antibacterial inhibition. A modified nucleic acid includes a deletion, addition and substitution of the nucleotide sequence, or a phosphorylation, alkylation, 2'-O-methyl substituted ribonucleotides phosphodiester and/or 3', 5' end-blocking etc. The specification only discloses a modified protonated oligonucleotide consisting of 2'-O-methyl substituted ribonucleotides phosphodiester and with both 3' and 5' butanol end-blocking which exhibits antibacterial activity. The specification indicates the nucleic acids with modified backbones such as phosphorothioates, methylphosphonates, 2-O-methylphosphorothioates, 2-O alkyl etc. are more resistant to nuclease or acid than their unmodified counterpart (specification, p. 9, lines 4-22). The unmodified protonated/acidified nucleic acids appear to be more susceptible to nuclease or acid degradation. The specification fails to provide specific guidance and evidence for whether the unmodified protonated/acidified nucleic acids would still retain the antibacterial activity as the modified protonated/acidified

nucleic acids as disclosed in the specification. Further, the protonated/acidified nucleic acids disclosed in the specification that shows antibacterial activities are monomers and oligomers up to about 12 nucleotides (SEQ ID No. 2). The claim encompasses protonated/acidified nucleic acid having hundreds or thousands of nucleotides. Since it requires adding acids, such as phosphoric acids, nitric acids, hydrochloric acids or acetic acids, to prepare protonated/acidified nucleic acids and unmodified nucleic acids are more susceptible to acid degradation, it is unclear how to prepare polymeric protonated/acidified nucleic acids longer than oligomers. The specification fails to provide specific guidance for how to prepare a polymeric protonated/acidified nucleic acid having hundreds or thousands of nucleotides and whether such nucleic acid would have antibacterial activity such that the wound dressing could provide wound healing function.

In view of the limitation of the pH value on the antibacterial activity of the nucleic acid, the lack of guidance regarding the stability and antibacterial activity of unmodified protonated/acidified nucleic acid, and the lack of guidance and evidence for how to obtain polymer protonated/acidified nucleic acid and whether said nucleic acid would have antibacterial activity, one skilled in the art at the time of the invention would not know how to use the full scope of wound dressing as claimed to provide wound healing function.

For the reasons set forth above, one skilled in the art at the time of the invention would have to engage in undue experimentation to practice over the full scope of the invention claimed. This is particularly true based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, the level of one of

ordinary skill which is high, the amount of experimentation required, and the breadth of the claims.

The quantity of the experimentation required to practice the claimed invention would include: trial and error experimentation to determine whether any unmodified protonated/acidified nucleic acid under any pH value could provide any antibacterial activity *in vivo*, trial and error experimentation to determine whether any modified protonated/acidified nucleic acid under a pH of greater than 4.5 could provide any antibacterial activity *in vivo*, preparation of modified and unmodified polymeric protonated/acidified nucleic acids having hundreds or thousands of nucleotides, trial and error experimentation to determine the antibacterial activity of said polymeric protonated/acidified nucleic acids, and trial and error experimentation to determine whether any protonated/acidified nucleic acid prepared from unmodified nucleic acids would have antibacterial activity.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER